Making more of oneself

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The game of life

By definition, all self-replicating things—cells, organisms, viruses, etc.—make more of themselves. Moreover, there is an inevitable trend towards being better at making more of themselves. We call this natural selection, but really it is just a statistical inevitability. Imagine a group of self-replicating things that were doing their thing, making more of themselves, when one of the new generations of self-replicating things became, for whatever reason, slightly better at making more of itself than the others in its cohort. Because it is more efficient at replicating itself, that new type of self-replicating thing will be a bit better represented in the next generation than the others of its cohort. That is, there will be more of it relative to the others. And its offspring's offspring will be even better represented, and so on down the generations. You can expect that pretty soon that new type will dominate the population. There was no intention to this, no trying to become better, no strategy, and certainly no thought about what was good for the population or "species" or things like that. This is simply what happens, on average, when there is a variant or type that is a bit better at making copies of itself than others[1]

[1] And this variation is heritable, or gets passed on to its offspring.

Evolution; it's inevitable. And this, gentle reader, is what we might call the game of life. So let's spend a bit of time thinking about what it means to make more of oneself.

The list of ingredients

When making something new,, one needs supplies. For a house one would need lumber, pipe, electric wire, nails, and a surprising number of doorknobs. But if we are making new cells[2] we need slightly different things: lipids, amino acids, deoxyribonucleic acids, sugars, and so on. In fact, we could (theoretically) come up with a list of ingredients to make a new cell[3]. What might be on this list?

[2] Or viruses

[3] It's worth noting that cells are not always identical—some are larger or smaller, some are specialized for energy production or lipid storage or structure. But while they differ, we could "average" across all of the cells of an organism to come up with a pretty decent ingredient list nonetheless.

You may recall from prior classes, some vague sense of "nutrition", or a text[4] a few bits. We could start with water, of course, which makes up $\geq 70\%$ of a cell's mass, and continue with:

[4] E.g., such as this wonderfully straightforward online book, The Cell: A Molecular Approach.

- Carbohydrates, from simple sugars, such as glucose, which is a primary energy store in cells, to polysaccharides, which both serve as the storage form of those simple sugars and form structural components of the cells. They are formed from a few (e.g., glucose has two, hexose has six) to many hundreds of CH_2O molecules strung together, occasionally with other groups for decoration[5].
- Lipids, which are predominant in cell membranes and vacuoles, store energy, and function in signaling[6]. These are usually a string of CH_2 (hydrocarbon) molecules] strung together in chains, sets of chains, or groups of rings. They

[5] Or function, I'm sure…I'm an ecologist, not a molecular biologist!

[6] Think steroid hormones, but also within-cell signally molecules

often have fancy terminal ends (e.g., a carboxyl group of COO^-) or heads (e.g., the phosphate groups, PO_4 in phospholipids that change their solubility in water, structure, capacity to interact with other molecules, and other things that influence their molecular biology.
- Nucleic acids—both RNA and DNA—that, well, you know what they do[7]. They are composed of purine and pyrimidine bases (one or two carbon rings with a couple of nitrogens in places of the carbons, plus more "decorations") attached to a sugar (ribose for RNA or 2'-deoxyribose for DNA).
- Amino acids form proteins, which are the most diverse category of molecule in the cell and also among the most important, servicing as structure, transport, and signally molecules, as well as catalyzing most every biochemical reaction. The amino acid backbone of the protein consist of a central Carbon atom bonded to a carboxyl group (COO^-), an amino group (NH_3), and a side chain that determines the molecule's function or capacity to interact with other molecules.

We can certainly find other basic molecules, but this short list comprises the vast majority of the cell's components.

Building from scratch

Again, we could theoretically take our list of ingredients, count how many glucoses and uracils and so on we needed to make a cell, and come up with a shopping list of sorts. We could even "build from scratch" by figuring out how many hydrogens we needed in all of the sugars and lipids and whatnot to get a more basic list of the numbers of each types of atom[8] that are required to build a new cell. After all, this is chemistry and at some level it is all interacting atoms. But we do not actually build our list of ingredients this way. For one, it would be tedious. And perhaps impossible[9].

If we are willing to build a list of atoms instead of molecules, we can simply[10] use <mumble, mumble> to measure the number of each element in a, say, gram of cells and get our materials list. For instance, I once used an atomic absorption spectrometer in science camp[11] to measure the elemental ratios of *Daphnia* spp. collected from the lake, which makes me think I'm not wholly out on a limb here. Anyway, people have done something like this and come up with the list of atoms that make up the vast, vast majority[12] of living tissues. The list is: C, H, N, O, P, S[13]].

This should make a bit of sense. Most of our list of molecules above involved one or a few hundred carbon atoms, many with hydrogens and oxygens attached. Plus there is all of the water. The phosphorus is not surprising if you simply think of ATP, but it is also important in nucleic acids, phospholipids, and more. The Sulfur is in the amino acids methionine and cysteine, but is also very common as a key part of enzymes[14].

I also want to add that there is a quite long list of other elements that are essential in small amounts to all life[15], or to particular types of life (e.g., Boron

[7] Or do you? Did you remember that adenosine 5'-triphosphate (ATP) is also a nucleotide? OK, full disclosure: I'd forgotten, too!

[8] Of course cells often do not work with actual atoms—if they obtain an amino acid they can use that amino acid as is, or at least convert it to one that is needed. But thinking of atoms is a reasonable way to proceed at a course level.

[9] I've been unable to find anyone that has actually done this. Let me know if you hear of such a study!

[10] Ha! Beware anyone that says something is "simple." That "simple" project might be a lifetime's work, or more!

[11] Yes, I was that kind of nerd. Although I honestly spent most of my time water skiing.

[12] Over 98% of us, and even more of bacteria!

[13] Pronounced CHNOPS. Also, it is worth noting that this ordering is not by mass or importance, but simply to get a lovely, pronounceable acronym. In fact oxygen is the most abundant atom in plants and animals.

[14] And if you're into extremophiles, sulfur can be the basis of metabolism, such as around back smoker vents at cracks in the ocean floor.

[15] E.g., Na, Mg, K, Ca, Cl, Mn, Fe, Cu, Zi, I, K, Fe. Google them to find out their various roles. They are quite interesting!

for plants, sodium and chlorine for animals[16], or silicon for diatoms). These are often called micronutrients because they are required in sometimes vanishingly small amounts. And again, remember that it is not necessarily the element that is important, but the molecule built from the elements. Vitamin C, for instance, is simply $C_6H_8O_6$—all of the stuff we normally take in with CHNOPS—but we[17] are unable to turn these elements we have in abundance into L-ascorbic acid. We must obtain it in its ready-to-use form. Our shortcut of simply counting atoms does not work universally, so take the next section with a grain of NaCl.

[16] Think of nerve impulses.

[17] And guinea pigs for reasons I do not understand.

Stoichiometry becomes useful

If we are willing to think of cells or larger organisms as sacks of chemical reactions—and *I* am, at least[18]—then our list of ingredients is something akin to the reactants on the left-hand side of a chemical reaction. (The cell or organism is, in a sense, the product on the right-hand side). What's more, we know the ratio of the different sorts of atoms required to make the cell or organism! This, my friend, is stoichiometry![19]

[18] Endless chains of chemical reactions where the product of one is a reactant to another. You have likely seen the citric acid or Krebs cycle, photosynthesis, protein synthesis, or any number of other reactions involved in life. That stuff—well, probably not photosynthesis!—is happening inside of us right now, as I write and you read.

[19] Please don't roll your eyes like that! In fact, you should go back to your chemistry instructor and tell them that they were, in fact, correct: stoichiometry did prove useful!

What can we do with this observation? Well, if we view life as (a series of highly complex) chemical reactions that occur within a lipid membrane, then all of the things you learned about chemistry apply to life, at least a this level of thinking. Perhaps most fundamentally we can see that if some reactant is limiting, it will slow or even stop a reaction from proceeding. Moreover, it is not the absolute amount of some reactants that matters, but the *ratio* of the reactants that is important: 12 oxygens per carbon, for instance.

We can go one step further: it turns out that the availability of elemental nutrients and their ratio can strongly influence which species grow best or are dominant in an area. At some level this is trivial; plants that require lots of N do not grow in places that do not have sufficient N whereas those that require less N or can create their own[20] can grow there. But even more nuanced relationships hold. Some *Daphnia* spp. are larger and slower growing than the fast-growing cyclopoid copepods[21]. While both feed directly on phytoplankton and have essentially the same structures and biochemistry, the stoichiometric ratios of elements they require are different. The copepods produce more ATP and more nucleic acids to fuel their rapid growth, which means they require more P for each N, whereas the daphnia are more protein-rich and thus require fewer P for each N. Thus if you fertilize the phytoplankton with P you end up favoring copepods over daphnia and if you you fertilize with N you favor daphnia over copepods. Elemental ratios helps determine who lives where (and when)![22]

[20] With the help of rhizobial bacteria, for instance.

[21] Both small, aquatic crustaceans.

[22] Please note that I am reconstructing this from my memory of the work from Jim Elser's lab at Arizona State University when I was a graduate student in the department, which was, as I write, quite some time ago! If you are interested, please look it up! It's cool work and I may have gotten some key details wrong. Plus, I know the work has advanced from there!

What is limiting?

One other lesson that comes from thinking of life as chemical reactions is the realization that *something* is always limiting. Always. If N is not limiting, then perhaps P is. If you have enough N and P, perhaps it is manganese or iron or even molybdenum. There is always *something* that is limiting the rate of the chemical reactions that are life. A consequence is that supplementing with a rate-limiting element or chemical only works until it is no longer limiting. Next time you go to the garden center look at the fertilizers they sell. Most include a particular ratio of N, P, and K (and sometimes a few other things). Now you know why.

Another consequence is that the waste of an organism can tell you something about what it does and does not need. Aphids, for instance, feed on the phloem of their host plant. This food source is largely photosynthates, like sucrose. That is, they are eating a high sugar diet. Indeed, they consume so much sugar that they are no longer energy limited, but by amino acids. Thus they excrete sugar water or "honeydew" that is often fed on by ants[23]. Similarly, animals that primarily eat plants, which are mostly carbon, leave waste that is mostly carbon after having taken up the materials they need to build more of themselves. Predators, on the other hand, often encounter so much nitrogen in their diets they poop out very nitrogen-rich feces, but much less carbon-poor. Building more of oneself is so amazing, right?

[23] Actually, the reality is more complex and neater. The sugars in the sap they feed on lead to high osmotic pressure in the aphids. They reduce this or osmoregulate by consuming the sugars and converting the sucrose to larger oligosaccharides that they excrete in the honey dew. So this is a more active process than a passive one I implied. Plus the honey dew can attract ants that provide protection for the aphids, so bonus! And lastly, the aphids rely on bacterial endosymbionts to produce most of the amino acids they need; and they feed them sugars. See wikipedia for a nice sketch of what's happening.